

### **REMARKS**

Claims 1, 6-8, 26-27 and 29-31 are presently pending. Claims 1 and 26 have been amended to overcome the claim objections related to non-overlapping steps, as suggested by the Examiner. No new matter has been added.

Claims 1 and 26 are objected to. Claims 1 and 26 are rejected as being indefinite. Claims 1, 6, 8, 26, 27, 29 and 31 are rejected as being anticipated and are also rejected as being obvious. Claims 7 and 30 are not rejected over the prior art, and thus are assumed to be clear of the prior art. Claims 1 and 6-8 are rejected for obviousness-type double patenting over various claims of Applicants' patent and pending applications. Each basis of rejection is separately addressed below.

#### **Claim Objections**

Claims 1, and 26 are objected to for the use of the terms "compound that inhibits" and "compound that promotes" respectively. The PTO asserts that the terms "inhibitor" or "promoter" would be more appropriate. Applicants respectfully disagree. First, Applicants fail to see any significant difference between a "compound that inhibits" and an "inhibitor" or between a "compound that promotes" and a "promoter". In either case the inhibitor or promoter is a "compound" that is identified as such according to the claimed assay. Second, the terms Applicants have employed are more consistent with the language of step (e) of claim 1 and claim 26. Accordingly, Applicants decline to make the suggested amendment.

Claims 1 and 26 are also objected to for the term "in the presence or absence of the compound", because non-overlapping steps are required. These claims have been amended to separate the treatment and assay steps in the presence of the test compound and in the absence of the test compound, as suggested by the Examiner. Applicants respectfully submit that these amendments overcome the objections to the claims and request that the objections be withdrawn.

#### **Indefiniteness**

Claims 1 and 26 are rejected as being indefinite for reciting the terms "expression of a cellular gene by p21 expression" and "the gene induced or repressed by p21". The rejection maintains that once the cellular genes are assayed, it is not possible to know how or what induced or repressed the expression. Since the specification clearly indicates that the gene that is

induced or repressed by p21 expression is known to be so induced or repressed, and the step of expressing p21 is included, claims 1 and 26 have been amended to recite that the gene to be assayed for expression is known to be induced or repressed by p21. Including a step to show that the gene expression is induced or repressed by p21 would allow a potential infringer to avoid infringement by using a gene that is known to be induced or repressed by p21 and reduce the value of the claim below what Applicants have contributed to the art. Applicants respectfully submit that this clarification overcomes the rejection and request that this rejection be withdrawn.

### **Anticipation**

Claims 1, 6, 8, 26, 27, 29, and 31 are rejected as anticipated by Fisher and Jiang (US 6,051,376). The rejection states that “MDA7 is taught is induced by induction of senescence ..., which is also associated with induction of p21 or mda6 ... . Identification of an inhibitor of MDA7, through identification of muted MDA7 expression, results in identification of inhibitors of p21 and senescence inherently.” (emphasis added)

The fact that MDA7 induction is “associated with”, or along with p21, however, does not mean that MDA7 is induced by p21, as required by claims 1 and 26. Fisher and Jiang do not teach or suggest that MDA7 is induced by p21, only that both p21 and MDA7 are both expressed in senescent cells. As discussed in the attached declaration of Dr. Roninson, the article by Chang et al. (2002), in which Dr. Roninson is a co-author, teaches that many of the genes that are induced in senescent HCT116 cells are induced independently of p21, although p21 is also induced in these cells. Dr. Roninson has also reviewed the results of his unpublished microarray analysis of the effect of IPTG-inducible p21 on the expression of all the known genes in HT1080 cells, with regard to the effects of p21 on MDA7 (now known as IL24) and found that p21 did not induce IL24 in HT1080 cells.

To anticipate a claimed invention, anticipation by the cited reference must be clear. Since Fisher and Jiang provides no evidence that MDA7 is actually induced by p21, as opposed to being expressed along with p21, and since MDA7 was not induced by p21 in HT1080 cells, Applicants respectfully submit that it is not at all clear that Fisher and Jiang anticipates claims 1 or 26, or their dependent claims. Applicants therefore respectfully request that this rejection be withdrawn.

**Obviousness**

Claims 1, 6, 8, 26, 27 and 29-31 are rejected as being obvious over Fisher and Jiang in view of Beug et al. The difference between this rejection and the anticipation rejection addressed above is that Fisher and Jiang do not teach that the assay uses a measure of gene product activity, and Beug et al is relied upon to provide this missing element in the obviousness rejection. As discussed above, Fisher and Jiang neither teaches nor suggests that MDA7 is actually induced by p21, and there is evidence to the contrary. Beug et al. provides nothing to overcome this deficiency. Accordingly, Applicants respectfully request that this rejection be withdrawn.

**Obviousness-type double patenting**

Claims 1 and 6-8 are rejected for obviousness-type double patenting over claims 1, 2, 4-8 and 11-14 of US Patent No. 6,706,491. Claims 1 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 38, 40, 44, 49-52 and 55-57 of co-pending application no. 10/233,032. Claims 1 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 25-30, 32, 33, 52-58, 95-101, 103-105 and 107-115 of co-pending application no. 09/861,925. Without admitting that claims 1 and 6-8 are obvious over the recited claims, and solely for the sake of expediting prosecution, Applicants submit herewith a terminal disclaimer over the cited patent and pending patent applications. Accordingly, Applicants respectfully request that this rejection be withdrawn.

**CONCLUSION**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner believes that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned attorney at 781-933-6630.

Respectfully submitted,

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